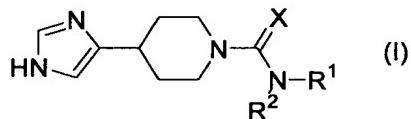


Claims

1. A preventive and/or therapeutic agent for neuropathic pain which comprises, as an active ingredient, a compound having histamine H3-receptor antagonism or a pharmaceutically acceptable salt thereof.
2. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having histamine H3-receptor antagonism is a compound represented by Formula (I):

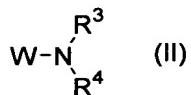


(wherein R¹ and R² may be the same or different and each represents a hydrogen atom, substituted or unsubstituted lower alkyl or substituted or unsubstituted cycloalkyl, or R¹ and R² are combined together with the adjacent nitrogen atom thereto to form a substituted or unsubstituted nitrogen containing-heterocyclic group; and X represents an oxygen atom or a sulfur atom).

3. The preventive and/or therapeutic agent for neuropathic pain according to Claim 2, wherein one of R¹ and R² is a hydrogen atom, and the other is substituted or unsubstituted lower alkyl or substituted or unsubstituted cycloalkyl, and X is a sulfur atom.
4. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having

histamine H3-receptor antagonism is thioperamide.

5. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having histamine H3-receptor antagonism is a compound represented by Formula (II):



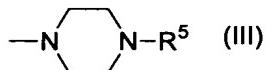
(wherein W represents a residue which imparts antagonistic and/or agonistic activity at histamine H3-receptors when attached to an imidazole ring in 4- or 5-position, and R³ and R⁴ may be the same or different and each represents substituted or unsubstituted lower alkyl or substituted or unsubstituted cycloalkyl, or R³ and R⁴ are combined together with the adjacent nitrogen atom thereto to form a substituted or unsubstituted nitrogen containing-heterocyclic group) or a pharmaceutically acceptable salt thereof.

6. The preventive and/or therapeutic agent for neuropathic pain according to Claim 5, wherein R³ and R⁴ may be the same or different and each is substituted or unsubstituted lower alkyl or substituted or unsubstituted cycloalkyl.

7. The preventive and/or therapeutic agent for neuropathic pain according to Claim 5, wherein R³ and R⁴ are combined together with the adjacent nitrogen atom thereto to form a substituted or unsubstituted nitrogen-containing

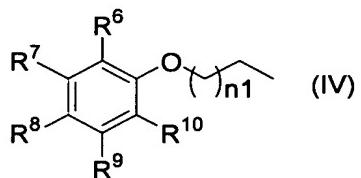
heterocyclic group.

8. The preventive and/or therapeutic agent for neuropathic pain according to Claim 5, wherein $-\text{NR}^3\text{R}^4$ is a group represented by Formula (III):



(wherein R⁵ represents lower alkyl, cycloalkyl, aryl, aralkyl, lower alkanoyl, cycloalkanoyl, aroyl, lower alkoxy carbonyl or aminoalkylcarbonyl).

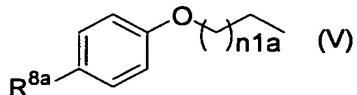
9. The preventive and/or therapeutic agent for neuropathic pain according to any of Claims 5 to 8, wherein W is a group represented by Formula (IV):



(wherein R⁶, R⁷, R⁸, R⁹ and R¹⁰ may be the same or different and each represents a hydrogen atom, halogen, amino, nitro, cyano, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkoxy, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted cycloalkanoyl, substituted or unsubstituted aroyl or substituted or unsubstituted lower alkanoylamino, and n1 represents an integer of 1 to 7).

10. The preventive and/or therapeutic agent for neuropathic pain according to any of Claims 5 to 8, wherein W is a group

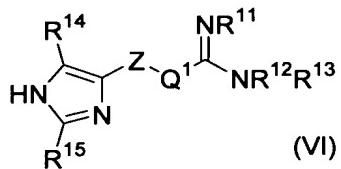
represented by Formula (V):



(wherein R^{8a} has the same meaning as R⁸ defined above, and n_{1a} has the same meaning as n₁ defined above).

11. The preventive and/or therapeutic agent for neuropathic pain according to Claim 10, wherein n₁ is 1 or 2.

12. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having histamine H₃-receptor antagonism is a compound represented by Formula (VI):

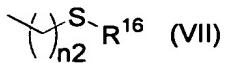


[wherein Z represents substituted or unsubstituted lower alkylene;

Q¹ represents a sulfur atom, -NH- or -CH₂-;

R¹¹, R¹³ and R¹⁵ may be the same or different and each represents a hydrogen atom, lower alkyl, cycloalkyl, substituted or unsubstituted aryl or substituted or unsubstituted aralkyl;

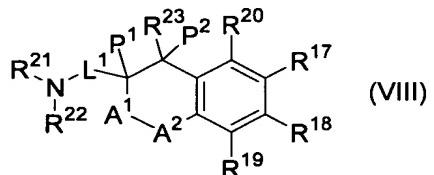
R¹² represents a hydrogen atom, lower alkyl, (cycloalkyl)alkyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl or a group represented by Formula (VII):



(wherein n₂ represents an integer of 1 to 4, and R¹⁶ represents lower alkyl, (cycloalkyl)alkyl or substituted or unsubstituted aralkyl); and R¹⁴ represents a hydrogen atom, halogen, amino, nitro, cyano, substituted or unsubstituted lower alkyl, substituted or unsubstituted aryl or substituted or unsubstituted aralkyl] or a pharmaceutically acceptable salt thereof.

13. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having histamine H3-receptor antagonism is clobenpropit.

14. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having histamine H3-receptor antagonism is a compound represented by Formula (VIII):



{ wherein A¹ represents a bond or carbonyl; A² represents an oxygen atom or a sulfur atom; L¹ represents lower alkylene which may be substituted by a fluorine atom or hydroxy; P¹ and P² represent hydrogen atoms or are combined to represent a bond;

R^{17} , R^{18} , R^{19} and R^{20} may be the same or different and each represents a hydrogen atom, halogen, nitro, hydroxy, mercapto, cyano, carboxy, lower alkanoyl, lower alkoxy carbonyl, lower alkanoyloxy, lower alkylthio, lower alkylsulfinyl, lower alkylsulfonyl, substituted or unsubstituted lower alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted lower alkoxy, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group, $-NR^{24a}R^{24b}$ (wherein R^{24a} and R^{24b} may be the same or different and each represents a hydrogen atom, lower alkyl or lower alkanoyl), $-C(=O)-NR^{24c}R^{24d}$ (wherein R^{24c} and R^{24d} have the same meanings as R^{24a} and R^{24b} defined above, respectively), $-SO_2-NR^{24e}R^{24f}$ (wherein R^{24e} and R^{24f} have the same meanings as R^{24a} and R^{24b} defined above, respectively), $-L^2-R^{25}$ [wherein L^2 represents an oxygen atom, a sulfur atom, lower alkylene, lower alkenylene, $-S(O)-$, $-S(O)_2-$, $-C(O)-$, $-C(=NOR^{26})-$ (wherein R^{26} represents a hydrogen atom or lower alkyl) or $-N(R^{27})-$ (wherein R^{27} represents a hydrogen atom, lower alkyl or lower alkanoyl), and R^{25} represents cycloalkyl, aryl or a heterocyclic group], or $-L^3-L^4-R^{28}$ [wherein L^3 represents cycloalkylene, arylene, a divalent group formed by removing any one hydrogen atom from an aliphatic heterocyclic group or heteroarylene, L^4 represents a bond, an oxygen atom, a sulfur atom, lower alkylene, lower alkenylene, $-C(O)-$,

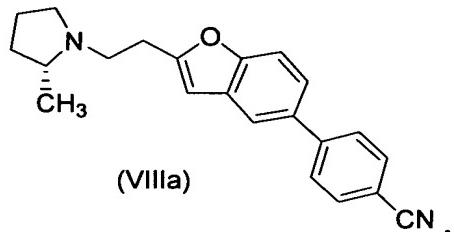
$-\text{C}(=\text{N}\text{OR}^{26a})-$ (wherein R^{26a} has the same meaning as R^{26} defined above) or $-\text{N}(\text{R}^{27a})-$ (wherein R^{27a} has the same meaning as R^{27} defined above), and R^{28} has the same meaning as R^{25} defined above] ; at least one of R^{17} , R^{18} , R^{19} and R^{20} represents cycloalkyl, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group, $-\text{L}^2\text{R}^{25}$ (wherein L^2 and R^{25} have the same meanings as defined above, respectively) or $-\text{L}^3\text{L}^4\text{R}^{28}$ (wherein L^3 , L^4 and R^{28} have the same meanings as defined above, respectively);

R^{21} and R^{22} may be the same or different and each represents a hydrogen atom, lower alkyl, hydroxy-lower alkyl, cycloalkyl, (cycloalkyl)alkyl, lower alkenyl, lower alkynyl, aryl, aralkyl, a heterocyclic group or heterocyclic alkyl, or R^{21} and R^{22} are combined together with the adjacent nitrogen atom thereto to form a substituted or unsubstituted nitrogen-containing heterocyclic group;

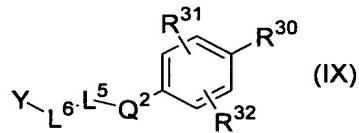
and R^{23} represents a hydrogen atom, halogen, nitro, hydroxy, mercapto, cyano, carboxy, lower alkoxycarbonyl, lower alkanoyl, lower alkanoyloxy, lower alkylsulfinyl, lower alkylsulfonyl, lower alkylthio, aryl, a heterocyclic group, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkoxy, $-\text{NR}^{29a}\text{R}^{29b}$ (wherein R^{29a} and R^{29b} have the same meanings as R^{24a} and R^{24b} defined above, respectively), $-\text{C}(=\text{O})-\text{NR}^{29c}\text{R}^{29d}$ (wherein R^{29c} and R^{29d} have the same meanings as R^{24a} and R^{24b} defined above, respectively) or

$-\text{SO}_2-\text{NR}^{29e}\text{R}^{29f}$ (wherein R^{29e} and R^{29f} have the same meanings as R^{24a} and R^{24b} defined above, respectively) } .

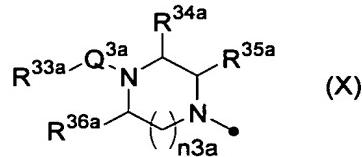
15. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having histamine H3-receptor antagonism is a compound represented by Formula (VIIIa) :



16. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having histamine H3-receptor antagonism is a compound represented by Formula (IX) :



{ wherein Y represents a group represented by Formula (X) :



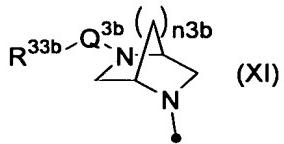
[wherein n_{3a} is 1 or 2;

Q^{3a} represents a bond, $-\text{C}(\text{O})-$, $-\text{C}(\text{S})-$, $-\text{CH}_2-$, $-\text{SO}_2-$ or $-\text{C}(=\text{N}\text{R}^{37})-$ (wherein R^{37} represents a hydrogen atom, hydroxy, lower alkyl, cycloalkyl, (cycloalkyl)alkyl, lower alkoxy,

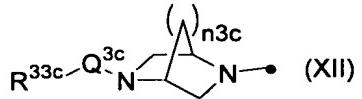
aryl or aralkyl);

R^{33a} represents a hydrogen atom, amino, lower alkyl, lower alkoxy, cycloalkoxy, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted aryloxy, a substituted or unsubstituted heterocyclic group or $-W^1-C(R^{38a})(R^{38b})-NR^{39a}R^{39b}$ (wherein W^1 represents a bond or substituted or unsubstituted lower alkylene, R^{38a} and R^{38b} may be the same or different and each represents a hydrogen atom, amino, aralkyl or substituted or unsubstituted lower alkyl, and R^{39a} and R^{39b} may be the same or different and each represents a hydrogen atom, aminosulfonyl, lower alkyl, lower alkanoyl, lower alkylsulfonyl, cycloalkyl, (cycloalkyl)alkyl, cycloalkanoyl, cycloalkylsulfonyl, aralkyl, aroyl, arylsulfonyl, heterocyclic alkyl, heterocyclic carbonyl, heterocyclic alkanoyl, heterocyclic sulfonyl, substituted or unsubstituted aryl, a substituted or unsubstituted aromatic heterocyclic group or a substituted or unsubstituted aliphatic heterocyclic group, or R^{39a} and R^{39b} are combined together with the adjacent nitrogen atom thereto to form a substituted or unsubstituted nitrogen-containing heterocyclic group, or R^{38a} or R^{38b} and R^{39a} or R^{39b} are combined together with the adjacent carbon atom and nitrogen atom thereto to form a substituted or unsubstituted heterocyclic group);

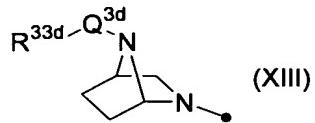
and R^{34a} , R^{35a} and R^{36a} may be the same or different and each represents a hydrogen atom or lower alkyl], a group represented by Formula (XI):



(wherein n_{3b} , Q^{3b} and R^{33b} have the same meanings as n_{3a} , Q^{3a} and R^{33a} defined above, respectively), a group represented by Formula (XII):



(wherein n_{3c} , Q^{3c} and R^{33c} have the same meanings as n_{3a} , Q^{3a} and R^{33a} defined above, respectively) or a group represented by Formula (XIII):



(wherein Q^{3d} and R^{33d} have the same meanings as Q^{3a} and R^{33a} defined above, respectively);

L^5 represents a bond or lower alkylene which may be substituted by substituted or unsubstituted aryl;

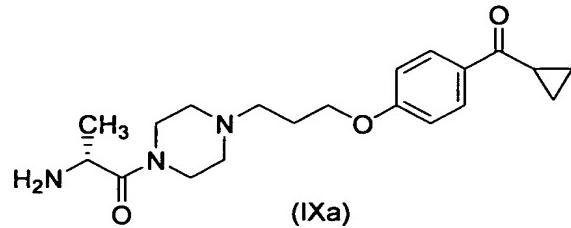
L^6 represents a bond, substituted or unsubstituted lower alkylene, or substituted or unsubstituted cycloalkylene, and L^5 and L^6 do not represent bonds simultaneously;

Q^2 represents an oxygen atom, a sulfur atom, $-S(O)-$, $-S(O)_2-$

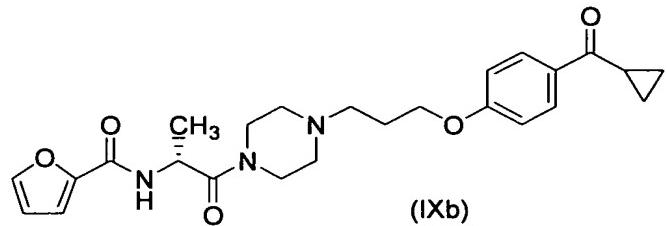
or $-C\equiv C-$;

R^{30} represents halogen, amino, cyano, aminocarbonyl, cycloalkyl, lower alkoxy, lower alkanoyl, cycloalkanoyl, lower alkoxycarbonyl, mono- or di(lower alkyl)aminocarbonyl, aralkyl, aroyl, arylsulfonyl, aromatic heterocyclic carbonyl, aromatic heterocyclic sulfonyl, substituted or unsubstituted lower alkyl, substituted or unsubstituted aryl, a substituted or unsubstituted aromatic heterocyclic group, $-CHR^{40a}-OR^{41a}$ (wherein R^{40a} represents a hydrogen atom, lower alkyl, cycloalkyl, (cycloalkyl)alkyl, aryl or aralkyl, and R^{41a} represents a hydrogen atom, lower alkyl, cycloalkyl, (cycloalkyl)alkyl, lower alkanoyl, lower alkoxycarbonyl, tri(lower alkyl)silyl, aryl or aralkyl), or $-C(R^{40b})=N-OR^{41b}$ (wherein R^{40b} and R^{41b} have the same meanings as R^{40a} and R^{41a} defined above, respectively); and R^{31} and R^{32} may be the same or different and each represents a hydrogen atom, halogen, amino, nitro, azido, hydroxy, cyano, formyl, carboxy, lower alkyl, perfluoro lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy or perfluoro lower alkoxy, or R^{31} and R^{32} are combined to represent $-OCH_2C(O)-\}$.

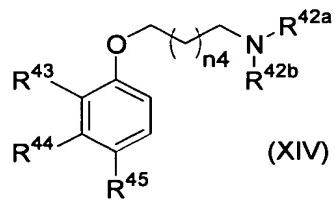
17. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having histamine H3-receptor antagonism is a compound represented by Formula (IXa):



18. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having histamine H3-receptor antagonism is a compound represented by Formula (IXb):



19. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having histamine H3-receptor antagonism is a compound represented by Formula (XIV):



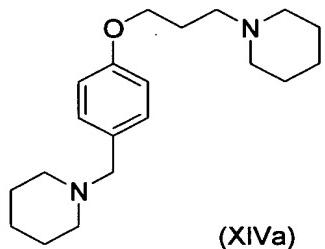
{ wherein n4 represents an integer of 0 to 4;
R^{42a} and R^{42b} may be the same or different and each represents lower alkyl, lower alkenyl, cycloalkyl or (cycloalkyl)alkyl,
or R^{42a} and R^{42b} are combined together with the adjacent nitrogen atom thereto to form a nitrogen-containing

heterocyclic group;

and two of R⁴³, R⁴⁴ and R⁴⁵ may be the same or different and each represents a hydrogen atom or halogen, and the remainder represents a substituted or unsubstituted heterocyclic group, substituted or unsubstituted heterocyclic alkyl, substituted or unsubstituted heterocyclic alkenyl, substituted or unsubstituted heterocyclic alkynyl, -L⁷-L⁸-Q⁴ [wherein L⁷ represents a bond or an oxygen atom, L⁸ represents substituted or unsubstituted lower alkylene, cycloalkylene, alkenylene or alkynylene, and Q⁴ represents an aliphatic heterocyclic group or -NR^{46a}R^{46b} (wherein R^{46a} and R^{46b} may be the same or different and each represents a hydrogen atom, lower alkyl, lower alkenyl, cycloalkyl, (cycloalkyl)alkyl, aryl, aralkyl, a heterocyclic group or heterocyclic alkyl)], -N(L^{8a}-Q^{4a})R⁴⁷ (wherein L^{8a} and Q^{4a} have the same meanings as L⁸ and Q⁴ defined above, respectively, and R⁴⁷ represents a hydrogen atom, lower alkyl, lower alkenyl, cycloalkyl, (cycloalkyl)alkyl, a heterocyclic group or heterocyclic alkyl) or -L⁹-C(L^{8b}-Q^{4b})R⁴⁸R⁴⁹ (wherein L^{8b} and Q^{4b} have the same meanings as L⁸ and Q⁴ defined above, respectively, L⁹ represents a bond, substituted or unsubstituted lower alkylene, cycloalkylene, alkenylene or alkynylene, R⁴⁸ represents a hydrogen atom, lower alkyl, lower alkenyl, cycloalkyl, (cycloalkyl)alkyl, a heterocyclic group or

heterocyclic alkyl, and R⁴⁹ represents a hydrogen atom, halogen, hydroxy or lower alkoxy}}.

20. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having histamine H3-receptor antagonism is a compound represented by Formula (XIVa):



21. A method for preventing and/or treating neuropathic pain, which comprises administering an effective amount of the compound having histamine H3-receptor antagonism.

22. The method for preventing and/or treating neuropathic pain according to Claim 21, wherein the compound having histamine H3-receptor antagonism is the compound described in any of Claims 2 to 20.

23. Use of a compound having histamine H3-receptor antagonism, for the manufacture of a preventive and/or therapeutic agent for neuropathic pain.

24. The use of a compound having histamine H3-receptor antagonism according to Claim 23, wherein the compound having histamine H3-receptor antagonism is the compound described in any of Claims 2 to 20.